disclose; **G. Hamilton**: Nothing to disclose; **A. Seifalian**: Nothing to disclose.

PS224.

Nogo-B Protein Modulates Intimal Thickening During Vein Graft Adaptation

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Objectives: Nogo-B is a protective factor in the vascular system, limiting the response to arterial injury. We hypothesized that Nogo-B would diminish in thickened vein grafts after exposure to arterial levels of pressure and shear stress. We examined the expression of Nogo-B, as well as its three receptors, Nogo-receptor (NgR), Nogo-B-receptor (NgBR), and PirB (Paired immunoglobulin-like receptor B), during mouse vein graft adaptation.

Methods: The intrathoracic inferior vena cava (IVC) of C57Bl/6 (WT) or Nogo-A/B knockout (Nogo-KO) mice was harvested and implanted as an interposition vein graft into WT mice. Vein grafts were harvested and analyzed after 3 weeks. mRNA transcript levels of Nogo-B, NgR, NgBR, PirB and GAPDH were measured by qPCR. Immunohistology (IHC) and Western blotting were performed using the antibodies: Nogo (N18: Santa Cruz), Nogo-B (1761), F4/80 (AbD serotec).

Results: All vein grafts showed significant wall thickening, with increased thickening in Nogo-KO compared to WT grafts ($0.125 \pm .025$ mm vs 0.043 ± 0.003 mm, $n = 4$; $p < 0.05$). In WT vein grafts, Nogo-B protein levels were strongly increased compared to preimplantation IVC (IHC density ~ 6-fold, Western blot density ~ 10-fold). Nogo-B RNA transcripts were increased 2-fold in the vein graft compared to IVC. Transcript levels of the NgR and NgBR were unchanged in vein grafts compared to IVC, whereas PirB transcript levels were increased approximately 20-fold ($n = 3$; $p < 0.05$).

Conclusions: Nogo-B transcripts and protein, as well as transcripts for its PirB receptor, were increased during vein graft adaptation, suggesting that graft adaptation is not a response to injury, but an adaptive remodeling response. Nogo-B is a factor limiting this adaptive response, and may signal via the PirB receptor. These results suggest that Nogo-B signaling is a mechanism of vein graft adaptation and might be a therapeutic target for human trials targeting vein graft disease.

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PS226.

Nitric Oxide Decreases the Expression of the 11S Proteasome Activator In Vivo

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Objectives: The 26S proteasome degrades the majority of proteins in eukaryotic cells. The 11S proteasome activator (PA28) binds to the proteasome and increases its ability to degrade small peptides. Expression of the PA28 subunits (α, β, γ) is induced by interferon-γ stimulation. Since inflammation plays a role in the development of neointimal hyperplasia, and since nitric oxide (NO) reduces neointimal hyperplasia in animal models, we hypothesize that NO will reduce the expression of PA28.

Methods: The carotid artery balloon injury model was performed in 11-week-old male Sprague Dawley rats. Treatment groups included injury or injury+PROLI/NO (20 mg). PA28 subunit expression was assessed by Western blot analysis on homogenized arteries excised 3 days after injury ($n = 3$/group) and by immunofluorescent staining of carotid artery sections harvested 14 days after injury ($n = 3$/group). Contralateral arteries served as uninjured controls.

Results: Following arterial injury, Western blot analysis showed that expression of the PA28α, β and γ subunits remained unchanged. However, after injury and treatment with NO, expression of the PA28α, β and γ subunits decreased substantially in the carotid artery lysates (1.9-, 2.3- and 3.4-fold, respectively). Immunofluorescence staining of carotid artery sections following injury revealed a slight increase in the expression of PA28α in the adventitia, perhaps due to multimeric PA28α binding the antibody more effectively. The expression of PA28β and γ following injury were relatively similar to control. NO significantly decreased the expression of PA28α in the media, whereas NO decreased the expression of PA28β and γ throughout the neointima, media and adventitia.

Conclusions: We report that NO decreased the expression of PA28 α, β and γ following arterial injury in vivo. Since the PA28 subunits are involved in the breakdown of peptides during inflammation, PA28 inhibition may be one mechanism by which NO inhibits neointimal hyperplasia.

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PS228.

Cilostazol Causes Angiogenesis Mediated Through the Enhancement of Nitric Oxide Production in Athe Ischemic Hindlimb of Mouse

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